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=> file hcaplus; d que l20; d que l24; d que l25; d que l30; d que l31
FILE 'HCAPLUS' ENTERED AT 11:25:50 ON 25 JUL 2003
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FILE COVERS 1907 - 25 Jul 2003  VOL 139 ISS 5
FILE LAST UPDATED: 24 Jul 2003  (20030724/ED)

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.
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L3	1946	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	SEROTONIN TRANSPORT?
L6	25962	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	TRANSPORT PROTEINS+OLD/CT
L9	1318836	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	MAMMAL/CT OR MAMMALIA/CT OR HUMAN
L15	5971	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	INSECT/CT OR INSECTA/CT
L16	6950	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	MANDUCA OR AEDES
L20	2	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L6 (L) L3 AND L9 AND (L15 OR L16)

L3	1946	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	SEROTONIN TRANSPORT?
L4	208686	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	BIOLOGICAL TRANSPORT+PFT/CT
L6	25962	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	TRANSPORT PROTEINS+OLD/CT
L9	1318836	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	MAMMAL/CT OR MAMMALIA/CT OR HUMAN
L15	5971	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	INSECT/CT OR INSECTA/CT
L16	6950	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	MANDUCA OR AEDES
L24	1	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	(L4 (L) L3) AND (L6 (L) L3) AND L9 AND (L15 OR L16)

L3	1946	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	SEROTONIN TRANSPORT?
L15	5971	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	INSECT/CT OR INSECTA/CT
L16	6950	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	MANDUCA OR AEDES
L25	4	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L3 AND (L15 OR L16)

L3	1946	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	SEROTONIN TRANSPORT?
L4	208686	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	BIOLOGICAL TRANSPORT+PFT/CT
L6	25962	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	TRANSPORT PROTEINS+OLD/CT
L26	212872	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	MAMMAL?
L29	17	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L3 AND L26 AND L4 AND L6
L30	5	SEA	FILE=HCAPLUS	ABB=ON PLU=ON	L29 AND (DROSOP? OR MAMMALIAN)

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L3          1946 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SEROTONIN TRANSPORT?
L4        208686 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BIOLOGICAL TRANSPORT+PFT/CT
L6         25962 SEA FILE=HCAPLUS ABB=ON  PLU=ON  TRANSPORT PROTEINS+OLD/CT
L26       212872 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MAMMAL?
L31            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (L4 (L) L3) AND (L6 (L) L3)
                  AND L26

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 FILE LAST UPDATED: 24 JUL 2003 (20030724/UP). FILE COVERS 1958 TO DATE.

 On April 13, 2003, MEDLINE was reloaded. See HELP RLOAD for details.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2003 vocabulary. See http://www.nlm.nih.gov/mesh/changes2003.html
 for a description on changes.

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L33         1159 SEA FILE=MEDLINE ABB=ON  PLU=ON  SEROTONIN TRANSPORTER/CN
L34       108492 SEA FILE=MEDLINE ABB=ON  PLU=ON  INSECTS+NT/CT
L35      2630958 SEA FILE=MEDLINE ABB=ON  PLU=ON  MAMMALS+NT/CT
L36            7 SEA FILE=MEDLINE ABB=ON  PLU=ON  L33 AND L34 AND L35

L33         1159 SEA FILE=MEDLINE ABB=ON  PLU=ON  SEROTONIN TRANSPORTER/CN
L42         6790 SEA FILE=MEDLINE ABB=ON  PLU=ON  INSECT PROTEINS+NT/CT
L43            1 SEA FILE=MEDLINE ABB=ON  PLU=ON  L33 AND L42


=> s l36 or l43
L57            7 L36 OR L43


=> file biosis; d que l47
FILE 'BIOSIS' ENTERED AT 11:26:47 ON 25 JUL 2003
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 23 July 2003 (20030723/ED)


L44       510908 SEA FILE=BIOSIS ABB=ON  PLU=ON  753?/BC
L45      1064186 SEA FILE=BIOSIS ABB=ON  PLU=ON  857?/BC
L46         2155 SEA FILE=BIOSIS ABB=ON  PLU=ON  SEROTONIN TRANSPORT?
L47            3 SEA FILE=BIOSIS ABB=ON  PLU=ON  L46 AND L45 AND L44
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=> file embase; d que l51
FILE 'EMBASE' ENTERED AT 11:26:53 ON 25 JUL 2003
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 FILE COVERS 1974 TO 24 Jul 2003 (20030724/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L48         1093 SEA FILE=EMBASE ABB=ON  PLU=ON  SEROTONIN TRANSPORTER/CT
L49        30149 SEA FILE=EMBASE ABB=ON  PLU=ON  MAMMAL/CT
L50         9506 SEA FILE=EMBASE ABB=ON  PLU=ON  INSECT/CT
L51            1 SEA FILE=EMBASE ABB=ON  PLU=ON  L48 AND L49 AND L50


=> file wpid; d que l55
FILE 'WPIDS' ENTERED AT 11:26:59 ON 25 JUL 2003
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FILE LAST UPDATED:          23 JUL 2003      <20030723/UP>
MOST RECENT DERWENT UPDATE:     200347        <200347/DW>
DERWENT WORLD PATENTS INDEX SUBSCRIBER FILE, COVERS 1963 TO DATE

>>> NEW WEEKLY SDI FREQUENCY AVAILABLE --> see NEWS  <<<

>>> PATENT IMAGES AVAILABLE FOR PRINT AND DISPLAY <<<

>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/dwpi/updates/dwpicov/index.html <<<

>>> FOR A COPY OF THE DERWENT WORLD PATENTS INDEX STN USER GUIDE,
    PLEASE VISIT:
 http://www.stn-international.de/training_center/patents/stn_guide.pdf <<<

>>> FOR INFORMATION ON ALL DERWENT WORLD PATENTS INDEX USER
    GUIDES, PLEASE VISIT:
    http://www.derwent.com/userguides/dwpi_guide.html <<<


L52           95 SEA FILE=WPIDS ABB=ON  PLU=ON  SEROTONIN (5A) TRANSPORT?
L53       233447 SEA FILE=WPIDS ABB=ON  PLU=ON  MAMMAL? OR HUMAN OR ANIMAL
L54        49401 SEA FILE=WPIDS ABB=ON  PLU=ON  INSECT? OR DROS? OR MOSQUITO OR
                 AEDES OR MANDUCA
L55            2 SEA FILE=WPIDS ABB=ON  PLU=ON  L52 AND L53 AND L54



=> dup rem l57 l56 l47 l51 l55
FILE 'MEDLINE' ENTERED AT 11:29:16 ON 25 JUL 2003

FILE 'HCAPLUS' ENTERED AT 11:29:16 ON 25 JUL 2003
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FILE 'BIOSIS' ENTERED AT 11:29:16 ON 25 JUL 2003
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FILE 'EMBASE' ENTERED AT 11:29:16 ON 25 JUL 2003

FILE 'WPIDS' ENTERED AT 11:29:16 ON 25 JUL 2003

PROCESSING COMPLETED FOR L57
PROCESSING COMPLETED FOR L56
PROCESSING COMPLETED FOR L47
PROCESSING COMPLETED FOR L51
PROCESSING COMPLETED FOR L55
L58 23 DUP REM L57 L56 L47 L51 L55 (3 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE MEDLINE
ANSWERS '8-19' FROM FILE HCAPLUS
ANSWERS '20-22' FROM FILE BIOSIS
ANSWER '23' FROM FILE EMBASE

=> d ibib ab l58 1-23

L58 ANSWER 1 OF 23 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2002424526 MEDLINE
DOCUMENT NUMBER: 22168984 PubMed ID: 12180970
TITLE: A cocaine insensitive chimeric insect serotonin transporter reveals domains critical for cocaine interaction.
AUTHOR: Sandhu Sumandeep K; Ross Linda S; Gill Sarjeet S
CORPORATE SOURCE: Environmental Toxicology Graduate Program and Department of Cell Biology and Neuroscience, University of California, Riverside 92521, USA.
CONTRACT NUMBER: AI 34524 (NIAID)
AI 48049 (NIAID)
SOURCE: EUROPEAN JOURNAL OF BIOCHEMISTRY, (2002 Aug) 269 (16) 3934-44.
Journal code: 0107600. ISSN: 0014-2956.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020816
Last Updated on STN: 20021011
Entered Medline: 20021010

AB Serotonin transporters are key target sites for clinical drugs and psychostimulants, such as fluoxetine and cocaine. Molecular cloning of a serotonin transporter from the central nervous system of the insect Manduca sexta enabled us to define domains that affect antagonist action, particularly cocaine. This insect serotonin transporter transiently expressed in CV-1 monkey kidney cells exhibits saturable, high affinity Na+ and Cl- dependent serotonin uptake, with estimated Km and Vmax values of 436 +/- 19 nm and 3.8 +/- 0.6 x 10-18 mol.cell.min-1, respectively. The Manduca high affinity Na+/Cl- dependent transporter shares 53% and 74% amino acid identity with the human and fruit fly serotonin transporters, respectively. However, in contrast to serotonin transporters from these two latter species, the Manduca transporter is inhibited poorly by fluoxetine (IC50 = 1.23 micro m) and cocaine (IC50 = 12.89 micro m). To delineate domains and residues that could play a role in cocaine interaction, the human serotonin transporter was mutated to incorporate unique amino acid substitutions, detected in the Manduca homologue. We identified a domain in extracellular loop 2 (amino acids 148-152), which, when inserted into the human transporter, results in decreased cocaine sensitivity of the latter (IC50 = 1.54 micro m). We also constructed a number of chimeras between the human and Manduca serotonin transporters

(hSERT and MasSERT, respectively). The chimera, hSERT1-146/MasSERT106-587, which involved N-terminal swaps including transmembrane domains (TMDs) 1 and 2, was remarkably insensitive to cocaine (IC50 = 180 micro m) compared to the human (IC50 = 0.431 micro m) and Manduca serotonin transporters. The chimera MasSERT1-67/hSERT109-630, which involved only the TMD1 swap, showed greater sensitivity to cocaine (IC50 = 0.225 micro m) than the human transporter. Both chimeras showed twofold higher serotonin transport affinity compared to human and Manduca serotonin transporters. Our results show TMD1 and TMD2 affect the apparent substrate transport and antagonist sensitivity by possibly providing unique conformations to the transporter. The availability of these chimeras facilitates elucidation of specific amino acids involved in interactions with cocaine.

L58 ANSWER 2 OF 23 MEDLINE on STN
ACCESSION NUMBER: 2001293139 MEDLINE
DOCUMENT NUMBER: 21264985 PubMed ID: 11062247
TITLE: Biophysical characterization of the cocaine binding pocket in the serotonin transporter using a fluorescent cocaine analogue as a molecular reporter.
AUTHOR: Rasmussen S G; Carroll F I; Maresch M J; Jensen A D; Tate C G; Gether U
CORPORATE SOURCE: Division of Cellular and Molecular Physiology, Department of Medical Physiology, The Panum Institute, University of Copenhagen, DK-2200 Copenhagen N, Denmark.
CONTRACT NUMBER: PO1 DA 12408 (NIDA)
R37 DA 05477 (NIDA)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Feb 16) 276 (7) 4717-23.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20030105
Entered Medline: 20010628

AB To explore the biophysical properties of the binding site for cocaine and related compounds in the serotonin transporter SERT, a high affinity cocaine analogue (3beta-(4-methylphenyl)tropane-2beta-carboxylic acid N-(N-methyl-N-(4-nitrobenzo-2-oxa-1,3-diazol-7-yl)ethanolamine ester hydrochloride (RTI-233); K(I) = 14 nm) that contained the environmentally sensitive fluorescent moiety 7-nitrobenzo-2-oxa-1,3-diazole (NBD) was synthesized. Specific binding of RTI-233 to the rat serotonin transporter, purified from Sf-9 insect cells, was demonstrated by the competitive inhibition of fluorescence using excess serotonin, citalopram, or RTI-55 (2beta-carbomethoxy-3beta-(4-iodophenyl)tropane). Moreover, specific binding was evidenced by measurement of steady-state fluorescence anisotropy, showing constrained mobility of bound RTI-233 relative to RTI-233 free in solution. The fluorescence of bound RTI-233 displayed an emission maximum (lambda(max)) of 532 nm, corresponding to a 4-nm blue shift as compared with the lambda(max) of RTI-233 in aqueous solution and corresponding to the lambda(max) of RTI-233 in 80% dioxane. Collisional quenching experiments revealed that the aqueous quencher potassium iodide was able to quench the fluorescence of RTI-233 in the binding pocket (K(SV =) 1.7 m(-)(1)), although not to the same extent as free RTI-233 (K(SV =) 7.2 m(-)(1)). Conversely, the hydrophobic quencher 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) quenched the fluorescence of bound RTI-233 more efficiently than free RTI-233. These data are consistent with a highly hydrophobic microenvironment in the binding pocket for

cocaine-like uptake inhibitors. However, in contrast to what has been observed for small-molecule binding sites in, for example, G protein-coupled receptors, the bound cocaine analogue was still accessible for aqueous quenching and, thus, partially exposed to solvent.

L58 ANSWER 3 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1999338325 MEDLINE
DOCUMENT NUMBER: 99338325 PubMed ID: 10404179
TITLE: Ionic interactions in the Drosophila serotonin transporter identify it as a serotonin channel.
AUTHOR: Petersen C I; DeFelice L J
CORPORATE SOURCE: Department of Pharmacology, Vanderbilt University Medical Center, Nashville, Tennessee 37232-6600, USA.
CONTRACT NUMBER: DA-07390 (NIDA)
NS-34075 (NINDS)
SOURCE: NATURE NEUROSCIENCE, (1999 Jul) 2 (7) 605-10.
Journal code: 9809671. ISSN: 1097-6256.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990816
Last Updated on STN: 19990816
Entered Medline: 19990802
AB Serotonin transporters (SERTs) are targets for drugs such as Prozac that increase serotonin (5HT) levels by blocking 5HT reuptake. Although SERTs saturate in the micromolar range, synaptic 5HT may exceed 1 mM. To examine SERT's response to high 5HT concentrations, we expressed Drosophila SERT (dSERT) in Xenopus oocytes and found that transport continued to increase with concentration up to 0.3 mM 5HT. As 5HT is a monovalent cation, its entry through an ion channel in SERT might explain uptake at high concentrations. We therefore investigated dSERT using traditional ion channel methods, including mole-fraction experiments under voltage clamp. We propose that SERTs may function as 5HT-permeable channels, and that this mechanism may be important for clearance of the neurotransmitter at high concentrations.

L58 ANSWER 4 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998452505 MEDLINE
DOCUMENT NUMBER: 98452505 PubMed ID: 9779469
TITLE: Structural determinants of neurotransmitter transport using cross-species chimeras: studies on serotonin transporter.
AUTHOR: Barker E L; Blakely R D
CORPORATE SOURCE: Department of Pharmacology, Vanderbilt University School of Medicine, Nashville, Tennessee 37232-6600, USA.
SOURCE: METHODS IN ENZYMOLOGY, (1998) 296 475-98.
Journal code: 0212271. ISSN: 0076-6879.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981216

L58 ANSWER 5 OF 23 MEDLINE on STN
ACCESSION NUMBER: 1998452502 MEDLINE
DOCUMENT NUMBER: 98452502 PubMed ID: 9779466
TITLE: Baculovirus-mediated expression of neurotransmitter

transporters.
AUTHOR: Tate C G
CORPORATE SOURCE: MRC Laboratory of Molecular Biology, Cambridge, United Kingdom.
SOURCE: METHODS IN ENZYMOLOGY, (1998) 296 443-55.
Journal code: 0212271. ISSN: 0076-6879.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY DATE: Entered STN: 19990115
Last Updated on STN: 19990115
Entered Medline: 19981216

L58 ANSWER 6 OF 23 MEDLINE on STN
ACCESSION NUMBER: 95014465 MEDLINE
DOCUMENT NUMBER: 95014465 PubMed ID: 7523405
TITLE: The effect of N-linked glycosylation on activity of the Na(+)- and Cl(-)-dependent serotonin transporter expressed using recombinant baculovirus in insect cells.
AUTHOR: Tate C G; Blakely R D
CORPORATE SOURCE: Medical Research Council Laboratory of Molecular Biology, Cambridge, United Kingdom.
CONTRACT NUMBER: DA 07390 (NIDA)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (1994 Oct 21) 269 (42) 26303-10.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199411
ENTRY DATE: Entered STN: 19941222
Last Updated on STN: 19960129
Entered Medline: 19941122

AB The rat Na(+)- and Cl(-)-dependent serotonin transporter was expressed in Sf9 insect cells using the baculovirus system. Expression of the serotonin transporter caused the Sf9 cells to accumulate [3H]serotonin (Km 78 nM) and to bind the specific transport inhibitor [125I]RT155 (2 beta-carbomethoxy-3 beta-(4-[125I]iodophenyl)tropane) (Kd 0.22 nM). Ligand binding assays on isolated membranes showed 500,000 copies of the serotonin transporter/cell (9 pmol/mg of membrane protein). Immunoreactive bands of apparent M(r) 54,000 (unglycosylated) and 60,000 (glycosylated) were observed in Western blots of membrane proteins from infected cells. The 54-kDa band was significantly smaller than the expected M(r) of 72,500 predicted from the cDNA sequence. The 54-kDa band was shown to represent the intact serotonin transporter by expressing a recombinant serotonin transporter that contained c-Myc and FLAG epitope tags engineered at the N and C termini, respectively. Both tags were present on a membrane protein that migrated slightly slower than the previously observed 54-kDa band, consistent with the extra mass added by the tags. The tags did not affect the Kd for [125I]RT155 binding. The effect of N-linked glycosylation on ligand binding and the level of expression were studied. The expression of the serotonin transporter in tunicamycin-treated Sf9 cells resulted in low levels of ligand binding activity (0.2 pmol/mg) but unchanged Kd. Similarly, mutated serotonin transporters that contained reduced numbers of N-linked glycosylation sites had unchanged Kd for [125I]RT155 binding whether there were 2, 1, or 0 N-linked glycosylation sites present on the serotonin transporter. In contrast, Bmax was dramatically reduced; levels of expression of the

unglycosylated serotonin transporter (0.4 pmol/mg) were 20-fold lower compared with levels of the fully glycosylated serotonin transporter. The Km for [3H]serotonin uptake was also unchanged. These data indicate that glycosylation is required for optimal stability of the serotonin transporter in the membrane but not for serotonin transport or ligand binding per se.

L58 ANSWER 7 OF 23 MEDLINE on STN
ACCESSION NUMBER: 94134723 MEDLINE
DOCUMENT NUMBER: 94134723 PubMed ID: 8302852
TITLE: A cocaine-sensitive Drosophila serotonin transporter: cloning, expression, and electrophysiological characterization.
AUTHOR: Corey J L; Quick M W; Davidson N; Lester H A; Guastella J
CORPORATE SOURCE: Division of Biology 156-29, California Institute of Technology, Pasadena 91125.
CONTRACT NUMBER: NS-11756 (NINDS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Feb 1) 91 (3) 1188-92. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-U02296
ENTRY MONTH: 199403
ENTRY DATE: Entered STN: 19940318
Last Updated on STN: 19940318
Entered Medline: 19940308

AB A cocaine-sensitive, high-affinity Drosophila serotonin (5-hydroxytryptamine; 5HT) transporter cDNA, denoted dSERT1, was isolated and characterized in oocytes. dSERT1 shows little transport of other monoamines and is Na+ and Cl- dependent. Sequence analysis indicates 12 putative transmembrane domains and strong homologies (approximately 50%) among dSERT1 and mammalian 5HT, norepinephrine, and dopamine transporters. Interestingly, the pharmacological properties of dSERT1, including sensitivity to antidepressants, are more similar to those of mammalian catecholamine transporters than to mammalian 5HT transporters. Two-electrode voltage-clamp analysis demonstrated 5HT-induced, voltage-dependent currents. Cloning and characterization of dSERT1 adds significantly to our knowledge of the diversity of 5HT transporters with regard to primary sequence, pharmacological profile, and permeation properties.

L58 ANSWER 8 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 1
ACCESSION NUMBER: 2002:754117 HCAPLUS
DOCUMENT NUMBER: 137:276105
TITLE: Use of **Manduca** sexta cell and **Aedes** aegypti membrane transporters as novel target sites for insecticides
INVENTOR(S): Gill, Sarjeet S.; Ross, Linda S.
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2002076204 A2 20021003 WO 2002-US8970 20020322
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2002197644 A1 20021226 US 2001-815923 20010323
PRIORITY APPLN. INFO.: US 2001-815923 A 20010323

AB The present invention discloses the existence of novel **Manduca** sexta cell and **Aedes** aegypti membrane transporters that can be used as targets for screening of new insecticides. This invention provides nucleic acids which encode the following insect cell membrane transporters: acetylcholine transporters, **serotonin transporters**, proline transporters, glutamate transporters, neurotransmitter transporters encoded by the inebriated gene, orphan transporters, GABA transporters, and LAT transporters. The invention also provides the polypeptides, cells expressing the polypeptides, and methods of using the nucleic acids and polypeptides to identify compds. which bind to or modulate the activity of the above-listed insect cell membrane transporters.

L58 ANSWER 9 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STNDUPLICATE 3
ACCESSION NUMBER: 1993:463999 HCAPLUS
DOCUMENT NUMBER: 119:63999
TITLE: **Serotonin transporter** cDNA and protein of rat and **human**
INVENTOR(S): Blakely, Randy D.; Caron, Marc G.; Fremeau, Robert T., Jr.
PATENT ASSIGNEE(S): Emory University, USA; Duke University
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9308261	A1	19930429	WO 1992-US9095	19921021
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, SE				
AU 9229116	A1	19930521	AU 1992-29116	19921021
PRIORITY APPLN. INFO.:			US 1991-778231	19911022
			WO 1992-US9095	19921021

AB CDNA and sequences for the **serotonin transporter** of rat and **human** are disclosed. Also disclosed are vectors and host cells contg. the DNA, methods of using them, purified protein, oligonucleotides, and antibodies which bind to the transporter protein. **Serotonin transporter** cDNA clone BS4E-10 was obtained from a rat brainstem cDNA library, sequenced, and expressed and characterized in HeLa fibroblasts. A structural model of the transporter is presented. **Human serotonin transporter** cDNA was also isolated, cloned, sequenced, and expressed in transfected HeLa cells. The gene was mapped to **human** chromosome 17.

L58 ANSWER 10 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:370290 HCAPLUS

DOCUMENT NUMBER: 137:104092
TITLE: Serotonin transporter function and pharmacology are sensitive to expression level. Evidence for an endogenous regulatory factor
AUTHOR(S): Ramsey, I. Scott; DeFelice, Louis J.
CORPORATE SOURCE: Department of Pharmacology, Center for Molecular Neuroscience, Vanderbilt University Medical Center, Nashville, TN, 37232-6600, USA
SOURCE: Journal of Biological Chemistry (2002), 277(17), 14475-14482
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE; English

AB We express **mammalian** serotonin transporters (SERTs) in Xenopus oocytes by cRNA injection and measure 5-hydroxytryptamine (5-HT) transport and 5-HT-induced current at varying expression levels. Transport and current both increase sigmoidally with the amt. of cRNA injected, but current requires apprx.5-fold more cRNA to elicit a half-maximal response. Western blots of SERT protein demonstrate that current, but not transport, correlates linearly with the amt. of SERT on the plasma membrane. In oocytes co-injected with wild-type SERT and an inactive SERT mutant, transport is similar to SERT alone, but current is attenuated. The charge/transport ratio reports the differential sensitivity of transport and current to increasing SERT cRNA injection and mutant co-expression. Manipulations that alter the charge/transport ratio also perturb substrate and inhibitor recognition. 5-HT, d-amphetamine, cocaine, and paroxetine inhibit transport more potently at lower expression levels; however, 5-HT potency for induction of current is similar at high and low expression. Moreover, the apparent potency of cRNA for transport depends on 5-HT concn. We postulate that SERT interacts allosterically with an endogenous factor of limited abundance to alter substrate and inhibitor potency and the balance of 5-HT transport and channel-like activity.

REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 11 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 2002:28544 HCAPLUS
DOCUMENT NUMBER: 136:210944
TITLE: Psychostimulants differentially regulate serotonin transporter expression in thalamocortical neurons
AUTHOR(S): Whitworth, Terri L.; Herndon, Laura C.; Quick, Michael W.
CORPORATE SOURCE: Department of Neurobiology, University of Alabama at Birmingham, Birmingham, AL, 35294, USA
SOURCE: Journal of Neuroscience (2002), 22(1), RC192/1-RC192/6
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB S-HT transporters (SERTs) are transiently expressed in thalamocortical neurons during development, permitting these glutamatergic neurons to co-release 5-HT as a "borrowed" transmitter. The high level of SERT expression in these neurons is likely important in the serotonergic modulation of neocortical circuits and provides a system for examg. endogenous SERT regulation. The authors tested the hypothesis that developmental expression of SERT in thalamocortical neurons is regulated by psychostimulants that are agonists and antagonists of SERT. Cultured thalamocortical neurons from embryonic day 18 rats were examd. for SERT

expression until postnatal day 15 (P15). In untreated cultures, SERT protein levels peaked at P3 and were absent by P10. Chronic treatment with SERT substrates (5-HT, 3,4-methylenedioxymethamphetamine) increased both peak SERT protein levels (4-fold) and the time course of SERT expression. SERT substrates also shifted the relative functional expression of SERT by redistributing intracellular SERT protein to the plasma membrane. The subcellular redistribution was prevented by PKC activators. SERT antagonists (e.g., fluoxetine, cocaine) reduced total SERT expression levels and the time course of SERT expression. These data show that: endogenous SERT is differentially regulated by 5-HT and psychostimulants; indicate that SERT modulation occurs via changes in both total SERT protein levels and subcellular redistribution of the transporter; and suggest that some of the actions of drugs of abuse in neocortical development may be attributable to alterations in SERT expression and concomitant changes in 5-HT signaling.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 12 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1998:522974 HCAPLUS
DOCUMENT NUMBER: 129:258072
TITLE: Localization and dynamic regulation of biogenic amine transporters in the **mammalian** central nervous system
AUTHOR(S): Hoffman, Beth J.; Hansson, Stefan R.; Mezey, Eva; Palkovits, Miklos
CORPORATE SOURCE: Unit on Molecular Pharmacology, Laboratory of Cellular and Molecular Regulation, National Institute of Mental Health, Bethesda, MD, 20892, USA
SOURCE: Frontiers in Neuroendocrinology (1998), 19(3), 187-231
CODEN: FNEDA7; ISSN: 0091-3022
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB This is a review with 211 refs. The monoamines, serotonin, dopamine, norepinephrine, epinephrine and histamine, play a crit. role in the function of the hypothalamic-pituitary-adrenal axis and in the integration of information in sensory, limbic, and motor systems. The primary mechanism for termination of monoaminergic neurotransmission is through reuptake of released neurotransmitter by Na+, CI-dependent plasma membrane transporters. A second family of transporters packages monoamines into synaptic and secretory vesicles by exchange of protons. Identification of those cells which express these two families of neurotransmitter transporters is an initial step in understanding what adaptive strategies cells expressing monoamine transporters use to establish the appropriate level of transport activity and thus attain the appropriate efficiency of monoamine storage and clearance. The most recent advances in this field have yielded several surprises about their function, cellular and subcellular localization, and regulation, suggesting that these mols. are not static and most likely are the most important determinants of extracellular levels of monoamines. Here, information on the localization of mRNAs for these transporters in rodent and human brain is summarized along with immunohistochem. information at the light and electron microscopic levels. Regulation of transporters at the mRNA level by manipulation in rodents and differences in transporter site densities by tomog. techniques as an index of regulation in human disease and addictive states are also reviewed. These studies have highlighted the presence of monoamine neurotransmitter transporters in neurons but not in glia in situ. The norepinephrine transporter is present in all cells which are both tyrosine hydroxylase (TH)- and dopamine .beta.-hydroxylase-pos. but not in those cells which are TH- and phenyl-N-methyltransferase-pos.,

suggesting that epinephrine cells may have their own, unique transporter. In most dopaminergic cells, dopamine transporter mRNA completely overlaps with TH mRNA-pos. neurons. However, there are areas in which there is a lack of one to one correspondence. The **serotonin transporter** (5-HTT) mRNA is found in all raphe nuclei and in the hypothalamic dorsomedial nucleus where the 5-HTT mRNA is dramatically reduced following immobilization stress. The vesicular monoamine transporter 2 (VMAT2) is present in all monoaminergic neurons including epinephrine- and histamine-synthesizing cells. Immunohistochem. demonstrates that the plasma membrane transporters are present along axons, soma, and dendrites. Subcellular localization of DAT by electron microscopy suggests that these transporters are not at the synaptic d. but are confined to perisynaptic areas, implying that dopamine diffuses away from the synapse and that contribution of diffusion to dopamine signalling may vary between brain regions. Interestingly, the presence of VMAT2 in vesicles underlying dendrites, axons, and soma suggests that monoamines may be released at these cellular domains. An understanding of the regulation of transporter function may have important therapeutic consequences for neuroendocrine function in stress and psychiatric disorders. (c) 1998 Academic Press.

REFERENCE COUNT: 213 THERE ARE 213 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L58 ANSWER 13 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:321589 HCAPLUS
DOCUMENT NUMBER: 127:47870
TITLE: **Drosophila serotonin transporters** have voltage-dependent uptake coupled to a serotonin-gated ion channel
AUTHOR(S): Galli, A.; Petersen, C. I.; deBlaquiere, M.; Blakely, R. D.; DeFelice, L. J.
CORPORATE SOURCE: Center Molecular Neuroscience, Department Pharmacology, Vanderbilt University Medical Center, Nashville, TN, 37232-6600, USA
SOURCE: Journal of Neuroscience (1997), 17(10), 3401-3411
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serotonin (5HT) transporters (SERTs) couple to existing ion gradients to transport 5HT into presynaptic terminals. In **mammalian** SERTs, the transport cycle is reported as electroneutral, with a translocation of zero net charge, and 5HT uptake is independent of membrane voltage. Yet **mammalian** SERTs exhibit 5HT-induced currents, and Drosophila SERTs (dSERTs) show voltage-dependent uptake. Thus, the relationship between uptake and current remains controversial; furthermore, the no. of 5HT mols. translocated per ion channel event is unknown. To investigate this, the authors have used heterologous expression of cloned dSERTs to measure 5HT flux and dSERT currents concurrently under voltage clamp, and the authors have used fluctuation anal. to measure the size of the elementary ionic events in the same cells. RNA-injected Xenopus oocytes accumulate 5HT, and paroxetine or desipramine inhibit this uptake. RNA-injected oocytes also display paroxetine-sensitive 5HT-induced currents and 5HT-independent leak currents. Na replacement decreases the uptake and the induced currents. 5HT-induced current and 5HT uptake both increase at neg. potentials, where 5HT carries .apprx.5% of the induced current. Recently, several groups have reported similar phenomena for other transporters, in which transmitter-induced currents exceed the predictions of coupled transport. The authors now provide evidence that in dSERT, .apprx.500 5HT mols. are translocated per channel opening, which, at -20

mV, carries .apprx.10,000 electronic charges. These data support a model in which 500 SERT cycles occur for each 5HT-induced channel opening or a model in which 500 5HT mols. and 10,000 electronic charges pass through a common pore.

L58 ANSWER 14 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1997:209096 HCAPLUS
DOCUMENT NUMBER: 126:288393
TITLE: H+ permeation and pH regulation at a **mammalian serotonin transporter**
AUTHOR(S): Cao, Yongwei; Mager, Sela; Lester, Henry A.
CORPORATE SOURCE: Division of Biology, California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: Journal of Neuroscience (1997), 17(7), 2257-2266
CODEN: JNRSDS; ISSN: 0270-6474
PUBLISHER: Society for Neuroscience
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rat **serotonin transporter** expressed in Xenopus oocytes displays an inward current in the absence of 5-HT when external pH is lowered to 6.5 or below. The new current differs from the leakage current described previously in two ways. It is .apprx. 10-fold larger at pH 5 than the leakage current at pH 7.5 and reaches 1000 H+/s per transporter at extremes of voltage and pH with no signs of satn. It is selective for H+ by reversal potential measurements. Similar H+-induced currents are also obsd. in several other ion-coupled transporters, including the GABA transporter, the dopamine transporter, and the Na+/glucose transporter. The high conductance and high selectivity of the H+-induced current suggest that protons may be conducted via a hydrogen-bonded chain (a "proton-wire mechanism") formed at least partially by side chains within the transporter. In addn., pH affects other conducting states of rat **serotonin transporter**. Acidic pH potentiates the 5-HT-induced, transport-assocd. current and inhibits the hyperpolarization-activated transient current. The dose-response relationships for these two effects suggest that two H+ binding sites, with pKa values close to 5.1 and close to 6.3, govern the potentiation of the 5-HT-induced current and the inhibition of the transient current, resp. These results are important for developing structure-function models that explain permeation properties of neurotransmitter transporters.

L58 ANSWER 15 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:580884 HCAPLUS
DOCUMENT NUMBER: 125:266409
TITLE: Expression and development of a functional plasmalemmal 5-hydroxytryptamine transporter by thyroid follicular cells
AUTHOR(S): Tamir, Hadassah; Hsiung, Shu-Chi; Liu, Kuo-Peing; Blakely, Randy D.; Russo, Andrew F.; Clark, Michael S.; Nunez, Eladio A.; Gershon, Michael D.
CORPORATE SOURCE: Div. Neurosci., New York State Psychiatric Inst., New York, NY, 10032, USA
SOURCE: Endocrinology (1996), 137(10), 4475-4486
CODEN: ENDOAO; ISSN: 0013-7227
PUBLISHER: Endocrine Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5-Hydroxytryptamine (5-HT) is synthesized and secreted by thyroid parafollicular (PF) cells. As all PF granules contain 5-HT, it is released whenever PF cells secrete. Because 5-HT stimulates follicular (F) cells and can modulate their response to TSH, 5-HT has been proposed

to be a paracrine PF to F cell transmitter. This role would require a thyroid mechanism to rapidly inactive 5-HT. A 5-HT transporter (SERT) in the plasma membrane of serotonergic neurons inactivates neuronal 5-HT. We thus tested the hypothesis that this mol. is expressed in the thyroid. The mRNA encoding SERT was demonstrated in both the human thyroid and a rat F cell (FRTL-5). SERT immunoreactivity was detected in rat F, but not PF, cells. Transporter-mediated uptake of [3H]5-HT by F cells arose early in development (E13 in mice) and was maintained in adult life in mice, guinea pigs, bats, and rats (FRTL-5 cells). These observations indicate that a functional SERT is expressed in the thyroid, not by the 5-HT-secreting PF cells, but by their putative F cell targets.

L58 ANSWER 16 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1996:756805 HCAPLUS
DOCUMENT NUMBER: 126:87553
TITLE: Single-channel currents produced by the serotonin transporter and analysis of a mutation affecting ion permeation
AUTHOR(S): Lin, Fan; Lester, Henry A.; Mager, Sela
CORPORATE SOURCE: Div. Biology, California Inst. Technology, Pasadena, CA, 91125, USA
SOURCE: Biophysical Journal (1996), 71(6), 3126-3135
CODEN: BIOJAU; ISSN: 0006-3495
PUBLISHER: Biophysical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Single-channel activities were obsd. in outside-out patches excised from oocytes expressing a **mammalian** 5-hydroxytryptamine (5-HT) transporter. Channel conductance was larger for a mutant in which asparagine177 of the third putative transmembrane domain was replaced by glycine, suggesting that this residue lies within or near the permeation pathway. The N177G mutant enables quant. single-channel measurements; it displays two conducting states. One state, with conductance of .apprx.6 pS, is induced by 5-HT and is permeable to Na+. The other state (conductance of .apprx.13 pS) is assocd. with substrate-independent leakage current and is permeable to both Na+ and Li+. Cl- is not a major current carrier. Channel lifetimes under all conditions measured are approx. 2.5 ms. The single-channel phenomena account for previously obsd. macroscopic electrophysiol. phenomena, including 5-HT-induced transport-assocd. currents and substrate-independent leakage currents. The channel openings occur several orders of magnitude less frequently than would be expected if one such opening occurred for each transport cycle and therefore do not represent an obligatory step in transport. Nevertheless, single-channel events produced by neurotransmitter transporters indicate the functional and structural similarities between transporters and ion channels and provide a new tool, at single-mol. resoln., for detailed structure-function studies of transporters.

L58 ANSWER 17 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1994:550109 HCAPLUS
DOCUMENT NUMBER: 121:150109
TITLE: Cloning, expression, and localization of a chloride-facilitated, cocaine-sensitive **serotonin transporter** from **Drosophila** melanogaster
AUTHOR(S): Demchyshyn, Lidia L.; Pristupa, Zdenek B.; Sugamori, Kim S.; Barker, Eric L.; Blakely, Randy D.; Wolfgang, William J.; Forte, Michael A.; Niznik, Hyman B.
CORPORATE SOURCE: Dep. Psychiatry, Univ. Toronto, Toronto, ON, M5S 1A8, Can.
SOURCE: Proceedings of the National Academy of Sciences of the

United States of America (1994), 91(11), 5158-62
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors report here on the isolation and characterization of a serotonin (5HT) transporter from Drosophila melanogaster. A 3.1-kb complementary DNA clone (dSERT) was found to encode a protein of 622 amino acid residues with a predicted mol. mass of .apprxeq.69 kDa and a putative transmembrane topol. characteristic of cloned members of the **mammalian** Na+/Cl- neurotransmitter cotransporter gene family. DSERT displays highest overall amino acid sequence identity with the **mammalian** 5HT (51%), norepinephrine (47%), and dopamine (47%) transporter and shares with all transporters 104 absolutely conserved amino acid residues. Upon transient expression in HeLa cells, dSERT exhibited saturable, high-affinity, and sodium-dependent [3H]5HT uptake with estd. Km and Vmax values of .apprxeq.500 nM and 5.2 .times. 10-18 mol per cell per min, resp. In marked contrast to the human SERT (hSERT), 5HT-mediated transport by dSERT was not absolutely dependent on extracellular Cl-, while the sodium-dependent uptake of 5HT was facilitated by increased extracellular Cl- concns. DSERT displays a pharmacol. profile and rank order of potency consistent with, but not identical to, **mammalian** 5HT transporters. Comparison of the affinities of various compds. for the inhibition of 5HT transport by both dSERT and hSERT revealed that antidepressants were 3- to 300-fold less potent on dSERT than on hSERT, while mazindol displayed .apprxeq.30-fold greater potency for dSERT. Both cocaine and RTI-55 inhibited 5HT uptake by dSERT with estd. inhibition consts. of .apprxeq.500 nM, while high concns. (>10 .mu.M) of dopamine, norepinephrine, octopamine, tyramine, and histamine failed to inhibit transport. In situ hybridization reveals the selective expression of dSERT mRNA to specific cell bodies in the ventral ganglion of the embryonic and larval Drosophila nervous system with a distribution pattern virtually identical to that of 5HT-contg. neurons. The dSERT gene was mapped to position 60C on chromosome 2. The availability of the gene encoding the unique ion dependence and pharmacol. characteristics of dSERT may allow for identification of those amino acid residues and structural motifs that confer the pharmacol. specificity and genetic regulation of the 5HT transport process.

L58 ANSWER 18 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN

ACCESSION NUMBER: 1994:290597 HCAPLUS
DOCUMENT NUMBER: 120:290597

TITLE: Conducting states of a **Mammalian serotonin transporter**

AUTHOR(S): Mager, Sela; Min, Churl; Henry, Douglas J.; Chavkin, Charles; Hoffman, Beth J.; Davidson, Norman; Lester, Henry A.
CORPORATE SOURCE: Div. Biol., California Inst. Technol., Pasadena, CA, 91125, USA

SOURCE: Neuron (1994), 12(4), 845-59
CODEN: NERNET; ISSN: 0896-6273
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have studied permeation at a cloned rat 5-HT transporter expressed in Xenopus oocytes. [3H]5-HT uptake and [125I]RTI-55 binding yield a turnover rate of .apprx. 1/s that does not depend on membrane potential. However, in voltage-clamp expts., three distinct currents result from 5-HT transporter expression. First, a steady-state, voltage-dependent transport-assocd. current is induced by 5-HT application. Second, a transient inward current is activated by voltage jumps to high neg. potentials in the absence of 5-HT and is blocked by 5-HT itself. Third, a small leakage current is obsd. in the absence of

5-HT. All the obsd. currents are blocked by inhibitors of 5-HT uptake but are differentially affected by Na+, Li+, K+, Ba2+, Cs+, Cl-, and amiloride. The conducting states of the 5-HT transporter may reflect the existence of a permeation pathway similar to that of ionic channels.

L58 ANSWER 19 OF 23 HCAPLUS COPYRIGHT 2003 ACS on STN
ACCESSION NUMBER: 1990:437897 HCAPLUS
DOCUMENT NUMBER: 113:37897
TITLE: High-affinity uptake a [3H]serotonin in cultured neurons of the cockroach Periplaneta americana
AUTHOR(S): Bermudez, Isabel; Beadle, David J.
CORPORATE SOURCE: Sch. Biol. Mol. Sci., Oxford Polytech., Oxford, UK
SOURCE: Archives of Insect Biochemistry and Physiology (1989), 12(4), 253-66
CODEN: AIBPEA; ISSN: 0739-4462
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cultured central neurons from the American cockroach, p. americana, were used to investigate the uptake of [3H]serotonin. The neurons accumulate [3H]serotonin from the extracellular medium by both a high- and a low-affinity system. The activity of the high-affinity mechanism is decreased by low temp. and metabolic poisons, and is dependent on Na+ and C-. Both depolarizing levels of external K+ and veratridine decrease the high-affinity uptake system, suggesting it is influenced by the transmembrane potential. The pyrethroid insecticides, deltamethrin and permethrin, enhance the inhibitory effect of veratridine. Pyrethroid enhancement is complete blocked by tetrodotoxin, and neither pyrethroid affects the uptake system in the absence of veratridine. Avermecin B1A is a powerful inhibitor of the high-affinity uptake system, and its effect is blocked by picrotoxin. High-affinity uptake of [3H]serotonin is inhibited by imipramine and amitriptyline; desipramine has no significant effect on this uptake. The activity of the high-affinity system is also reduced by 8-hydroxy-dipropylaminotetralin, .alpha.-methyl-serotonin, and 1-(3-chlorophenyl)piperazine. Dopamine, noradrenaline, octopamine, and the formamidine insecticides, chlordimeform and demethylchlordimerform, are moderate inhibitors of the high-affinity uptake system. The formamidine effect is not blocked by tetrodotoxin or picrotoxin.

L58 ANSWER 20 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:540674 BIOSIS
DOCUMENT NUMBER: PREV200100540674
TITLE: SERT biosynthesis and the problems of overexpression for structural studies.
AUTHOR(S): Tate, C. G. (1); Baker, C.; Williams, D. C.
CORPORATE SOURCE: (1) MRC Laboratory of Molecular Biology, Hills Road, Cambridge, CB2 2QH UK
SOURCE: Biochemical Society Transactions, (2001) Vol. 29, No. 5, pp. A95. print.
Meeting Info.: 674th Meeting of the Biochemical Society Dublin, Ireland July 11-13, 2001
ISSN: 0300-5127.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

L58 ANSWER 21 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:61940 BIOSIS
DOCUMENT NUMBER: PREV200000061940
TITLE: Identification of neurotransmitter transporters from Drosophila melanogaster.
AUTHOR(S): Porzgen, P. (1); Sonders, M. S. (1); Reed, A. I. (1);

Ingram, S. L. (1); Amara, S. G. (1)
CORPORATE SOURCE: (1) Howard Hughes Medical Institute, Oregon Health Sciences University, Vollum Institute L-474, Portland, OR USA
SOURCE: Society for Neuroscience Abstracts, (1999) Vol. 25, No. 1-2, pp. 160.
Meeting Info.: 29th Annual Meeting of the Society for Neuroscience, Part 1 Miami Beach, Florida, USA October 23-28, 1999 The Society for Neuroscience.
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English

L58 ANSWER 22 OF 23 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1975:209243 BIOSIS
DOCUMENT NUMBER: BA60:39239
TITLE: **SEROTONIN TRANSPORT** BY CULTURED BOVINE AORTIC ENDOTHELIUM.
AUTHOR(S): SHEPRO D; BATBOUTA J C; ROBBLEE L S; CARSON M P; BELAMARICH F A
SOURCE: CIRC RES, (1975) 36 (6), 799-806.
CODEN: CIRUAL. ISSN: 0009-7330.
FILE SEGMENT: BA; OLD
LANGUAGE: Unavailable

L58 ANSWER 23 OF 23 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V. on STN
ACCESSION NUMBER: 2001304173 EMBASE
TITLE: Overexpression of mammalian integral membrane proteins for structural studies.
AUTHOR: Tate C.G.
CORPORATE SOURCE: C.G. Tate, MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, United Kingdom. cgt@mrc-lmb.cam.ac.uk
SOURCE: FEBS Letters, (31 Aug 2001) 504/3 (94-98).
Refs: 53
ISSN: 0014-5793 CODEN: FEBLAL
PUBLISHER IDENT.: S 0014-5793(01)02711-9
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Recent successes in the determination of atomic resolution structures of integral membrane proteins have relied on purifying the proteins from abundant natural sources. In contrast, the majority of mammalian receptors, ion channels and transporters need to be overexpressed to obtain sufficient material for structural studies. This has often proved to be very difficult. Overexpression studies on a wide range of mammalian membrane proteins have shown that a few can be expressed functionally in bacteria, but many others require an insect or mammalian cell host for activity or high level expression. The serotonin transporter, which has been expressed in all the major hosts available, is a good example that has given insights into the problem of overexpressing mammalian membrane proteins for structural studies.

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